REMARKS

Upon entry of the foregoing amendments, claims 76 – 79, 84 – 85 and 101 – 110 are under consideration.

Applicants have amended claim 85 to better define the physiological consequence of the administration of the ubiquitin fusion protein provided in step (a) of Claim 84. Specifically, amended claim 85 now recites that the physiological consequence is "immunocastration." Support for this amendment can be found in the Specification as originally filed, and specifically at pg. 20, line 25 through pg. 21, line 2; and in Example 6 at pg. 45, line 25 through pg. 46, line 11. Applicants have also added new claims 101 – 110. New claims 101 – 104 incorporate the subject matter of original Claim 87, as included through the recitation of cancelled claims 1, 20, 41 and 58. New claims 105 – 110 are dependent on new claims 101 – 104 and are identical to original claims 88 – 93, which are now cancelled.

The present amendments add no new matter.

CLAIM OBJECTIONS

The Examiner has objected to claims 87 – 93 because claim 87 and corresponding dependent claims 88 – 93, are dependent on canceled claims 1, 20, 41 and 58.

Applicants have canceled claims 87 – 93 and replaced them with new claims 101 – 104, which incorporate the subject matter of original claim 87, as well as cancelled claims 1, 20, 41 and 58. New claims 105 – 110 are dependent on new claims 101 – 104 and are identical to original claims 88 – 93, which are now cancelled.

Accordingly, Applicants believe that the present objection is moot in light of the present amendment.

OBJECTION TO THE SPECIFICATION

The Examiner has objected to the Specification because it lacks specific reference to the appropriate priority documents upon which the present Application's priority claim is based. The

Examiner has objected to the amendment to the Specification filed on December 6, 2001, referenced in December 30, 2002 Office Action as "The amendment to the specification filed on 04 January 2002, in Paper NO:4, has not been entered, because it is improper."

Applicants have amended the Specification in order to incorporate a specific reference to US Patent Application No. 09/026,276, from which the present Application is a divisional application. Applicants have also amended the Specification to incorporate the unentered December 6, 2001 amendments made in Paper No. 4. Specifically, additions are indicated by underlining, while deletions are indicated by strikethrough, as permitted by the "Prototype Announcement" regarding Amendment format (*see e.g.* 1265 Off. Gaz. Pat. Office 87 (Dec. 17, 2002)). A Substitute Specification is attached.

Accordingly, Applicants believe that the present objections are now moot.

THE §112, SECOND PARAGRAPH REJECTIONS

The Examiner has rejected claims 77 – 79, 85 and 87 – 93 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Specifically, the Examiner stated that it is unclear as to how many epitopes are attached to ubiquitin and to which one the immune response would be directed.

Applicants note that the present invention is directed to methods using a "engineered" ubiquitin fusion protein that contains at least one "epitope-containing-segment" which includes at least one epitope. Thus, the ubiquitin fusion protein can contain more than one "epitope-containing-segment," either in a contiguous position (*i.e.*, adjacent to one another) or in a non-contiguous position (*i.e.*, separated by native ubiquitin amino acid sequence). As defined by the Specification, an epitope is a "recombinant immunologically active heterologous antigen." The "epitope-containing-segment" can contain more than one epitope, and preferably contains at least two epitopes. These multiple epitopes can be identical or they can be distinct. However, as taught in the Specification, there is no "theoretical limit on the number of epitopes which can be inserted within or fused to the N and C-terminus of a ubiquitin fusion protein." *See e.g.*, Specification at pg. 16, lines 25-29.

The Examiner also stated that it is also unclear, in the case of two or more non-identical epitopes, whether each epitope would elicit its own immune response.

In the case of a ubiquitin fusion protein that contains two or more distinct epitopes, the Specification clearly teaches that:

> [A]ntibodies produced following vaccination are specific for a single epitope and do not cross-react with other epitopes which have also been internally fused to ubiquitin. Thus, each epitope elicits a specific antibody response by producing antibodies which do not cross-react with other epitopes contained within the same ubiquitin fusion protein.

Id at pg. 16, line 32 through pg. 17, line 3.

The Examiner also stated that claim 85, in its recitation of "substantially similar", is indefinite.

Applicants have amended claim 85 to no longer recite the phrase "substantially similar." Specifically, Applicants have amended claim 85 to better define the physiological consequence of the administration of the ubiquitin fusion protein provided in step (a) of Claim 84. Specifically, amended claim 85 now recites that the physiological consequence is "immunocastration." Support for this amendment can be found in the Specification as originally filed, and specifically at pg. 20, line 25 through pg. 21, line 2; and in Example 6 at pg. 45, line 25 through pg. 46, line 11.

The Examiner has further maintained that claim 87 and corresponding dependent claims 88 – 93, in their dependency from canceled claims 1, 20, 41, and 58, recite "one, tow [*sic*] or more identical or non identical epitopes." Specifically, the Examiner states that "it is unclear, the level of which epitope should be reduced, after the administration of ubiquitin fusion proteins comprising more than one epitope into an animal."

Applicants disagree. First, Applicants would like to reiterate that claims 87 – 93 have been canceled and replaced with new claims 101 – 104, which incorporate the subject matter of original claim 87, as well as cancelled claims 1, 20, 41 and 58. New claims 105 – 110 are

dependent on new claims 101 – 104 and are identical to original claims 88 – 93, which are now cancelled.

Second, Applicants would like to clarify that canceled claim 87 and new claims 101 – 104, are directed to methods "for reducing levels of a *predetermined* protein" through the administration of a ubiquitin fusion protein containing at least one epitope, as described and taught by the present invention. The predetermined protein which is being reduced can be a peptide hormone (new claim 105), a tumor necrosis factor (new claim 108) or even a growth hormone protein (new claim 109). Thus, no epitopes are being reduced.

Accordingly, in light of the present amendments and arguments, Applicants respectfully request reconsideration and withdrawal of this basis of rejection.

ALLOWABLE SUBJECT MATTER

Applicants acknowledge the Examiner's allowance of claims 76 and 84.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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